

### **REMARKS**

Responsive to the Office Action mailed on January 24, 2003, Applicants have presented new dependent claims 23-35 directed to other aspects of the invention and/or the teachings in the specification of the above-captioned patent application.

Support for the new dependent claims can be found in the specification at least at page 19, line 21 through page 20, line 3; page 50, line 15 through page 52, line 5; and Figures 48 and 49.

#### **The New Matter Objection**

Applicants note that the Examiner has refused to enter their proposed amendment to the specification on the grounds that the amendment introduces new matter. The Examiner relied upon an "admission" purportedly to be found in the original language concerning the state of the prior art.

It is Applicants' position that no admission was ever made, and further that the amendment to the specification does not constitute new matter, but rather such amendment was made to correct a typographical error in the original specification. This position is supported by the original specification which refers to the prior art devices as microchip-based, not monolithic. In reference to the Examiner's comments at paragraph 1 of the outstanding Office action, the definitions provided support Applicants' position. The electrospray device of the present invention is monolithic in that it refers to a single block of material. In contrast, as noted by the Examiner, the Karger device is composed of component parts and therefore, is not monolithic.

At about the same time that the amendment to the specification was entered in connection with this matter, the same amendment was entered in all of the various related applications (the original application and all of the related divisionals). Three of the divisionals have now issued with the amendment to the specification (Patent Nos. 6,563,111; 6,569,324; and 6,579,452, copies of which are attached as Exhibits 1, 2, and 3). Applicants submit that the approval of the amendment in connection with these copending cases supports their view that no new matter was entered and that the amendment was made for the purpose of correcting a typographical error. In addition, Applicants submit that it would be improper for the instant parent application to have a

specification that is different from that of the first issued patents arising from its divisional offspring. Accordingly, Applicants respectfully request the Examiner to reconsider the rejection of the proposed amendment to the specification.

Moreover, to the extent that the current rejection of claim 10 under 35 U.S.C. 103(a) relies upon the “admission” of Applicants which have been both denied as having been admitted and the clarification of which is the subject of the proposed amendment to the specification, once the amendment is entered, there is no basis for this rejection. Further, Applicants’ denial that such admission has been made also makes it improper for the Examiner to rely upon such a purported admission in rejecting the claims. Accordingly, Applicants request that the rejection of the pending claims based thereon be withdrawn and the claims be found allowable.

#### The Provisional Double Patenting Rejection

Original claim 10 was rejected under the judicially created doctrine of obviousness-type double patenting as being obvious over claims 13-14 of U.S. Patent No. 6,245,227 (hereinafter sometimes referred to as the “227 patent”).

By way of background, the present application and the ‘227 patent share an identical specification. However, Kionix filed the application for the ‘227 patent independently of Advion based upon Kionix’s belief that only Kionix employees were inventors of the claims of the ‘227 patent. The parent of the present divisional application was filed jointly by Advion and Kionix based upon Applicants’ belief that employees of each company were inventors. Advion did not know that Kionix had filed the application for the ‘227 patent at the time of filing. Advion subsequently filed a lawsuit against Kionix and initiated an interference to have inventorship considered with respect to related applications.

In light of these developments Applicants suggest that the most reasonable course would be to stay consideration of the merits of any such double patenting rejection pending resolution of the lawsuit and/or interference while moving forward with the examination of the substantive prior art issues raised by the outstanding Office Action.

#### The Obviousness Rejection

Claim 10 was rejected under 35 U.S.C. § 103(a) as being obvious over WO 97/04297 to Karger et al. (“Karger”) in view of Miura or U.S. Patent No. 4,209,696 to Fite (“Fite”), and Applicants’ purported admission of the prior art as described on page 8, line 24 to page 10,

line 15 of the instant specification.

Claim 10 relates to an electrospray device including a monolithic substrate having a plurality of entrance orifices on an injection side and a plurality of nozzles on an ejection surface on an opposite planar side from the injection side, a plurality of channels each extending continuously through the monolithic substrate in communication with one of the plurality of entrance orifices and a corresponding one of the plurality of nozzles, and a region surrounding each nozzle recessed from the ejection surface. The plurality of nozzles are disposed in an array for ejecting a plurality of analytes at a mass spectrometry device interface. The electrospray device also includes a plurality of electrodes for the application of electric potentials for generating and controlling an electric field at each nozzle to direct the ejection of the analytes from the nozzles within an acceptance region of the mass spectrometry device. The electrospray device is formed monolithically from, for example, a monocrystalline silicone substrate, during the course of and as a result of a fabrication sequence that requires no manipulation or assembly of separate components. This enables the production of a device which is easily reproducible and manufacturable in high volumes. The region surrounding the nozzle recessed from the ejection surface enables the production of a durable nozzle having the physical asperity on which a large electric field may be concentrated. In this manner efficient and controllable electrospray can be achieved.

Karger relates to a microscale fluid handling system having channels etched in the surface of the substrate. The channels are subsequently covered with a separately machined cover plate, thereby defining covered on-substrate channels. The channels may be filled with membrane or packing material to carry out sample manipulations. The end of the channels may be microfabricated to form an electrospray exit port or tip that permits transfer of ions into the sampling orifice of a mass spectrometer by microelectrospray.

Karger discloses the following electrospray exit ports and nozzles: a flat edge-substrate exit port, as shown in Figure 1A; a pointed edge-substrate exit port defined by a sloped recess cut in the substrate between adjacent exit ports, as shown in Figure 1A; a nozzle tip extending outwardly from the surface of a separate cover plate, as shown in Figures 2B, 2C; and a nozzle formed within a recess within a separate cover plate, as shown in Figure 2D.

The Examiner cites the present specification at page 8, line 24 to page 10, line 15, particularly page 10, lines 9-11 for the proposition that applicants admit that the Karger prior art

substrate is a monolithic substrate.

Miura relates to a method and apparatus for ink jet printing and nozzles for use therein. The print head is constructed of a separately machined front nozzle plate secured to a rear nozzle plate. The rear nozzle plate has a nozzle projecting into an air chamber between the rear and front nozzle plates. The projecting nozzle can be formed with an annular groove to entrap liquid which might spill over the edge of the nozzle if an excessive amount of force is externally applied to the print head. The projecting nozzle is axially aligned with a channel in the front plate. A ring electrode secured to the front plate encircles the front channel. Liquid is forced from the projecting nozzle by the combined effects of electric field and pressure gradients to form a meniscus in the air chamber which is pulled forward to eject droplets of liquid through the front channel.

Miura fails to disclose or suggest a monolithic electrospray substrate. Rather, Miura discloses an ink jet printer print head constructed of a separately machined front nozzle plate secured to a rear nozzle plate.

The monolithic substrate of the present invention includes a channel extending continuously through the substrate in communication with the entrance orifice and the nozzle on the ejection surface. In contrast, Miura discloses a front channel and a rear channel separated by an air chamber. Ink passes from the rear channel through the rear nozzle, air chamber, and front channel where droplets are expelled from the front nozzle.

Further, Miura fails to disclose an electrospray substrate that ionizes analytes in the fluid for later detection by a mass spectrometer. In contrast, Miura relates to an ink jet printer nozzle which dispenses relatively larger non-ionized droplets of ink for printing. In this regard, applicants submit that the electrospray features of the present invention are not disclosed in or achievable by the rear nozzle plate 7 of Miura. The disclosure is not operable for ionizing analytes for detection by mass spectrometry.

Fite relates to a method and apparatus for mass spectrometry analysis of liquids which uses electrospray to form the molecular ions. Fluid is electrosprayed from the end of a capillary tube. Figures 5A to 5E teach several tip configurations for the capillary tube. Figure 5D shows a capillary tube tip having a flat end with the plane of the flat end being perpendicular to the axis of the capillary. Figure 5C shows a capillary tube tip having a flat end which has the outside edge removed to form an annular bevel. The tip configuration shown in Figure 5C allows

electrospray to be formed using lower voltages than that required by the tip configuration shown in Figure 5D.

The Examiner has argued that it “would have been obvious to one of ordinary skill in the art at the time the invention was made to extend the recess taught by Karger so that it surrounds the exit port as taught by Fite or Miura because as taught by Fite and Miura it would reduce the voltage needed to produce the electrospray and as taught by Miura an annular groove would entrap any spilled liquid from the nozzle.”

Applicants traverse this argument for at least the following reasons, and regard the Examiner’s argument with respect to the specification and claims as not establishing a *prima facie* case of obviousness of the claimed subject matter. Applicants do not admit that the Karger substrate is monolithic. The specification has been amended to correct an obvious typographical error at the location cited by the Examiner. In the original specification as filed, page 10, lines 9-11 incorrectly refers to the above-described prior art devices as edge-spraying from a “monolithic” chip, which has been corrected to read “microchip.” This correction is clearly supported throughout the specification. Each of the above-described prior art devices are described at page 8, lines 25 and 28; page 9, lines 3, 6, 8, 16, 18, 21 and 22; and page 10, lines 2 and 5 as a “microchip.” As noted above, Karger expressly describes the substrate as being constructed from separately machined parts in which a cover plate is placed over surface channels. Accordingly, it is clear that as filed the present specification contains a typographical error and not an admission as suggested by the Examiner.

Karger discloses channels etched in the surface of the substrate which are covered with a separately machined cover plate, thereby defining covered on-substrate channels. In contrast, the pending claims are, in part, directed to providing an electrospray device comprising “a plurality of channels each extending continuously through the monolithic substrate in communication with one of the plurality of entrance orifices and a corresponding one of the plurality of nozzles.” Providing such a through-substrate channel in a monolithic substrate enables the improved monolithic nozzle design described above that is durable and predictable, and is suitable to mass production.

Further, the pending claims are, in part, directed to an electrospray device having “a region surrounding each nozzle recessed from the ejection surface.” As noted above, Karger fails to disclose a nozzle surrounded by the claimed recessed region. The presently claimed

nozzle design provides the physical asperity required to produce sufficient electric field lines to effectively control the electrospray. Such a nozzle also obviates the fabrication problems associated with attaching tips to the substrate, as disclosed in Karger. As noted by the Examiner, Karger fails to teach that the recessed portion completely surrounds the exit ports or that the substrate is a monolithic substrate.

For at least the reasons noted above, there is no motivation to modify the electrospray device of Karger to arrive at the present invention absent applicants' disclosure. Since Karger relates to an electrospray device made from separate component parts, there is no motivation to manufacture the device from a monolithic substrate. Further, there is no suggestion how the device of Karger could be fabricated from a monolithic substrate. With respect to the presently claimed nozzle, there is no motivation to modify the many embodiments of the Karger nozzles to arrive at the claimed structure. There is no teaching in Karger of the relationship of nozzle shape to field line generation. Therefore, there is no motivation to extend the recess between exit ports to circumscribe the nozzle in order to provide a nozzle from which electrospray can be reliably controlled.

Moreover, neither Miura nor Fite make up for the deficiencies of Karger with respect to the lack of teaching or suggesting a monolithic substrate having the claimed features of the present invention. Miura discloses a component ink jet printer nozzle and Fite discloses a conventional capillary tube equipped electrospray device. Thus, even if the prior art teachings are combined in the manner suggested by the Examiner, the claimed invention is not provided.

There is no motivation to combine the teachings of the prior art in the manner suggested by the Examiner. Miura provides no motivation to extend the recess taught by Karger so that it surrounds the exit port. Miura teaches that the projecting nozzle in combination with the dead air region adjacent the exit end of the rear channel, the swirling pressurized air, and the electric field gradient electrostatically pull the liquid from the rear channel into a pencil-like shape and eject droplets through the front channel. The formation of the pencil-like shape of the liquid reduces the minimum voltage required to tear it into droplets. Karger relates to a different environment, i.e., creating an electrospray of ionized species, which does not include providing swirling air in a dead air region between a rear and front channel. Therefore, there would be no expectation of any advantage in extending the recess of Karger in the context of electrospray. Moreover, the annular groove taught by Miura to collect overflow of liquid only makes sense for

an ink jet printer nozzle which does not have source liquid volume limitations that are commensurate with the ionization of small volumes of samples by an electrospray nozzle.

Fite teaches that the tip configuration shown in Figure 5C is preferred over that shown in Figure 5D; however, capillary tube tip configuration is directed to nozzle shape, which is different from the structure of the region between the ejection surface and the nozzle. Fite merely teaches nozzle profile, i.e., a change in nozzle shape, and is silent with respect to region between the nozzle and the ejection surface.

Accordingly, for at least the reasons noted above, the proposed combination of Karger in view of Miura or Fite and applicants' admission fails to render obvious the presently claimed invention. Claims 23-35 depend from claim 10 and are patentable over the cited prior art for the same reasons as claim 10, as well as in view of the additional limitations of each of these claims. Withdrawal of the record rejection and allowance of claims 10 and 23-35 is respectfully requested.

Applicants believe the present response sets forth a showing of the differences between the present claims and the teachings and suggestions of the prior art establishing the patentability thereof. In the event the Examiner notes any remaining impediment that may be susceptible to resolution via a conference, a telephone call to Applicants' attorney is requested.

Dated this 18<sup>th</sup> day of July, 2003.

Respectfully submitted,



David O. Seeley

Attorney for Applicant

Registration No. 30,148

Holme Roberts & Owen LLP

299 South Main, Suite 1800

Salt Lake City, UT 84111

801-521-5800